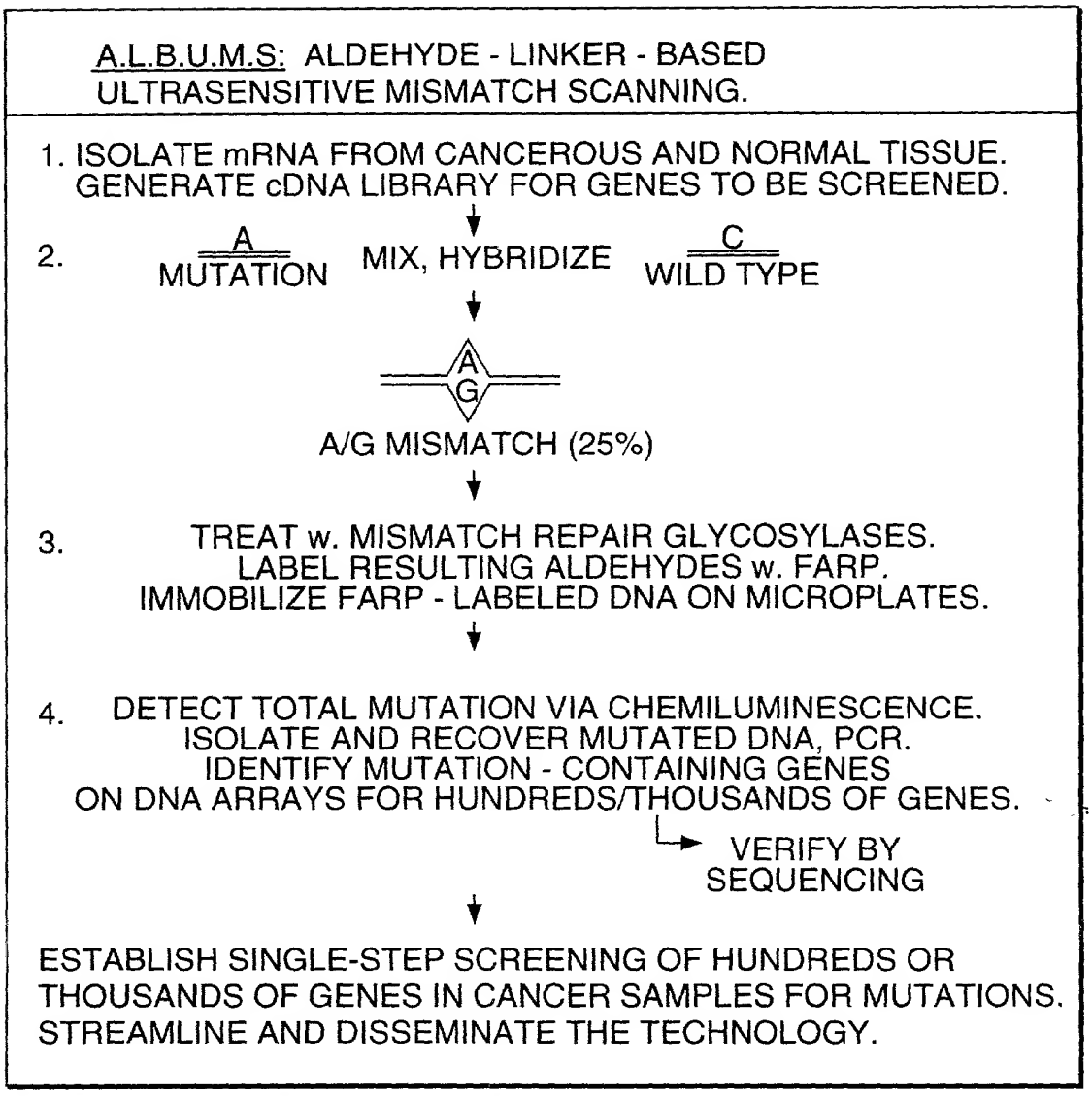


FIG. 1

TECHNOLOGY FOR ISOLATING AND IDENTIFYING MUTATIONS OVER HUNDREDS OR THOUSANDS OF GENES SIMULTANEOUSLY: AN EXAMPLE OF SCREENING FOR A-TO-C TRANSVERSIONS.

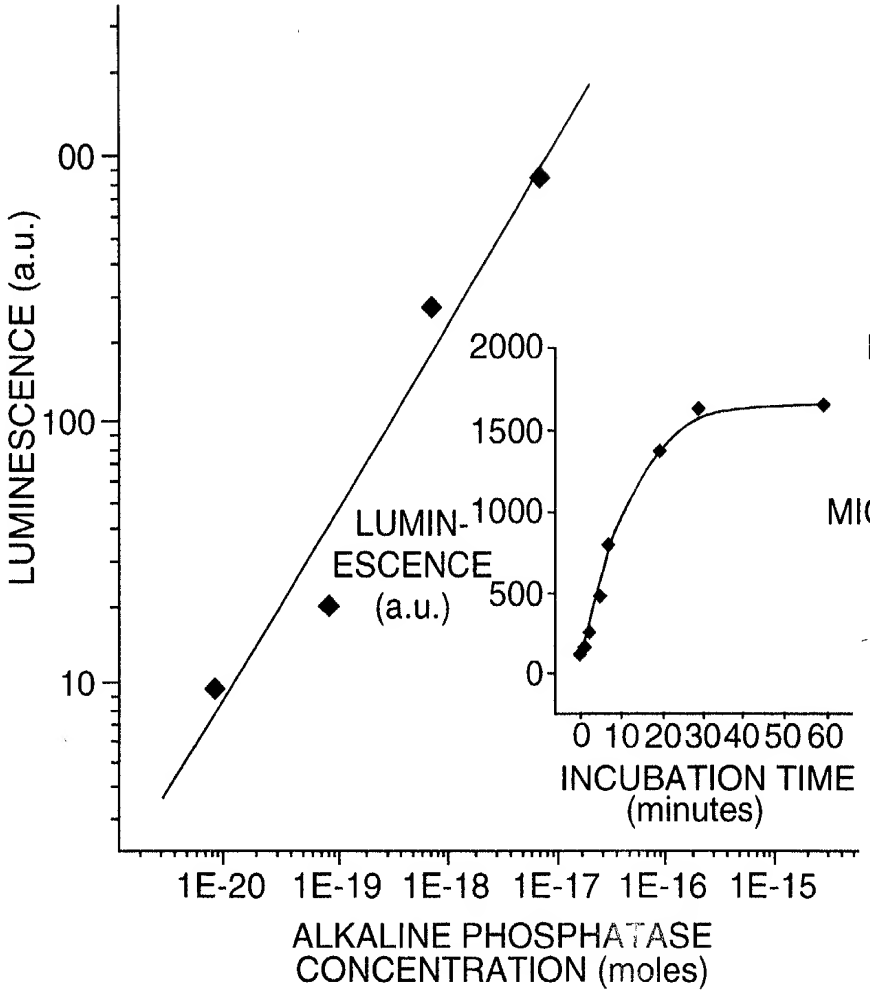

LUMINESCENCE (a.u.)
00
100
10
1E-20 1E-19 1E-18 1E-17 1E-16 1E-15
ALKALINE PHOSPHATASE CONCENTRATION (moles)
LUMIN-ESCENCE (a.u.)
2000
1500
1000
500
0
0 10 20 30 40 50 60
INCUBATION TIME (minutes)

FIG. 2A

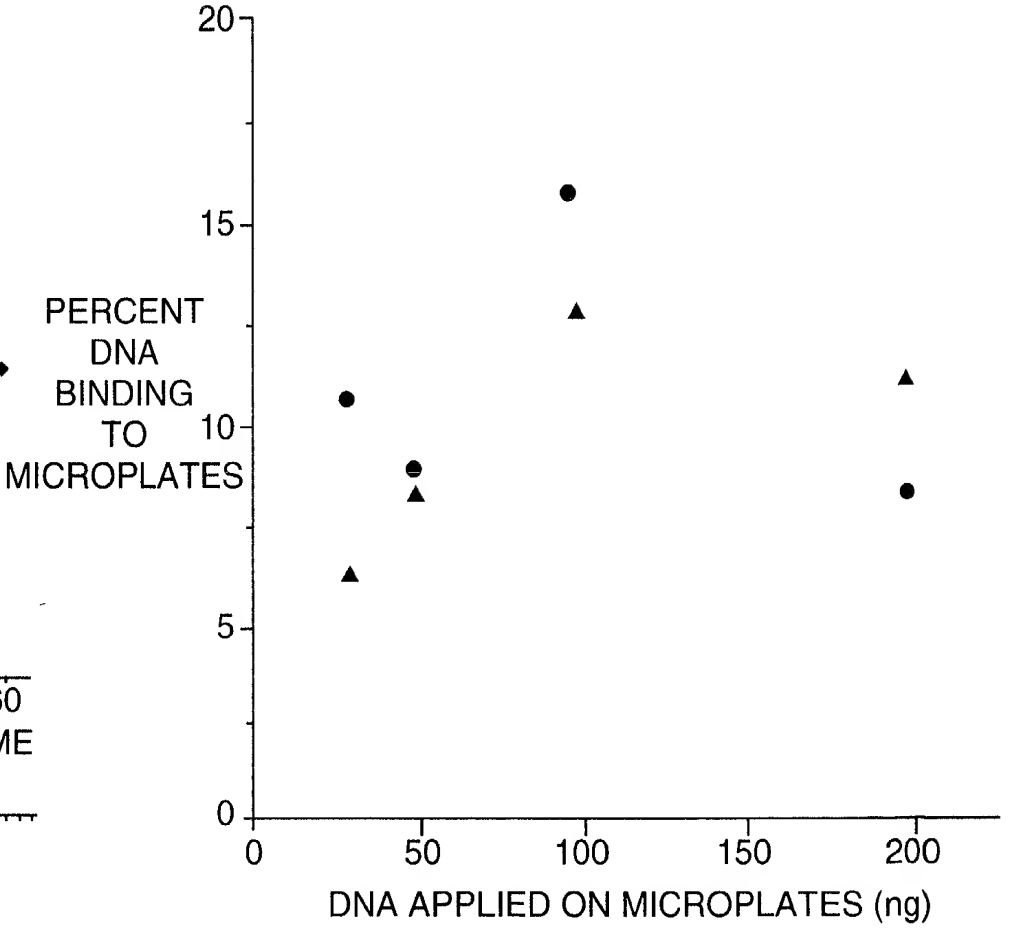

PERCENT DNA BINDING TO MICROPLATES
20
15
10
5
0
0 50 100 150 200
DNA APPLIED ON MICROPLATES (ng)

FIG. 2B

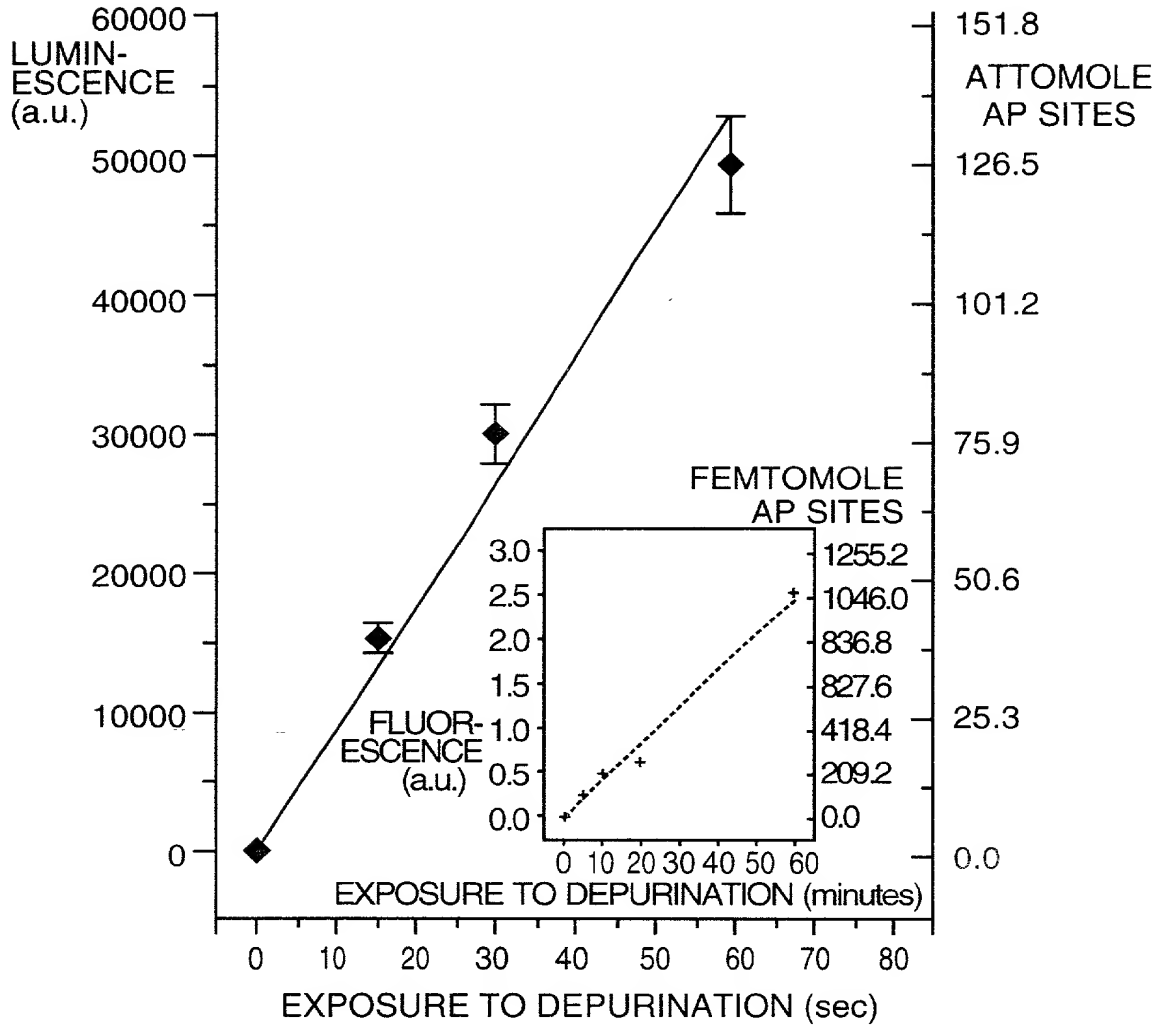

60000
LUMIN-
ESCENCE
(a.u.)
50000
40000
30000
20000
10000
0
151.8
ATTOMOLE
AP SITES
126.5
101.2
75.9
50.6
25.3
0.0
FEMTOMOLE
AP SITES
3.0
2.5
2.0
1.5
1.0
0.5
0.0
FLUOR-
ESCENCE
(a.u.)
1255.2
1046.0
836.8
827.6
418.4
209.2
0.0
0 10 20 30 40 50 60
EXPOSURE TO DEPURINATION (minutes)
0 10 20 30 40 50 60 70 80
EXPOSURE TO DEPURINATION (sec)

FIG. 3

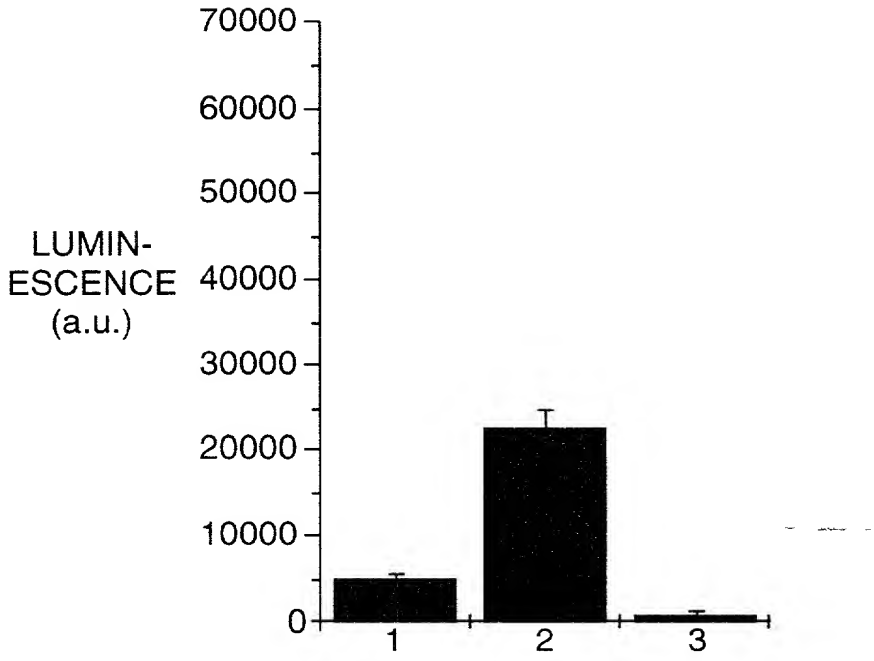

LUMIN-
ESCENCE
(a.u.)
70000
60000
50000
40000
30000
20000
10000
0
1
2
3

FIG. 4A

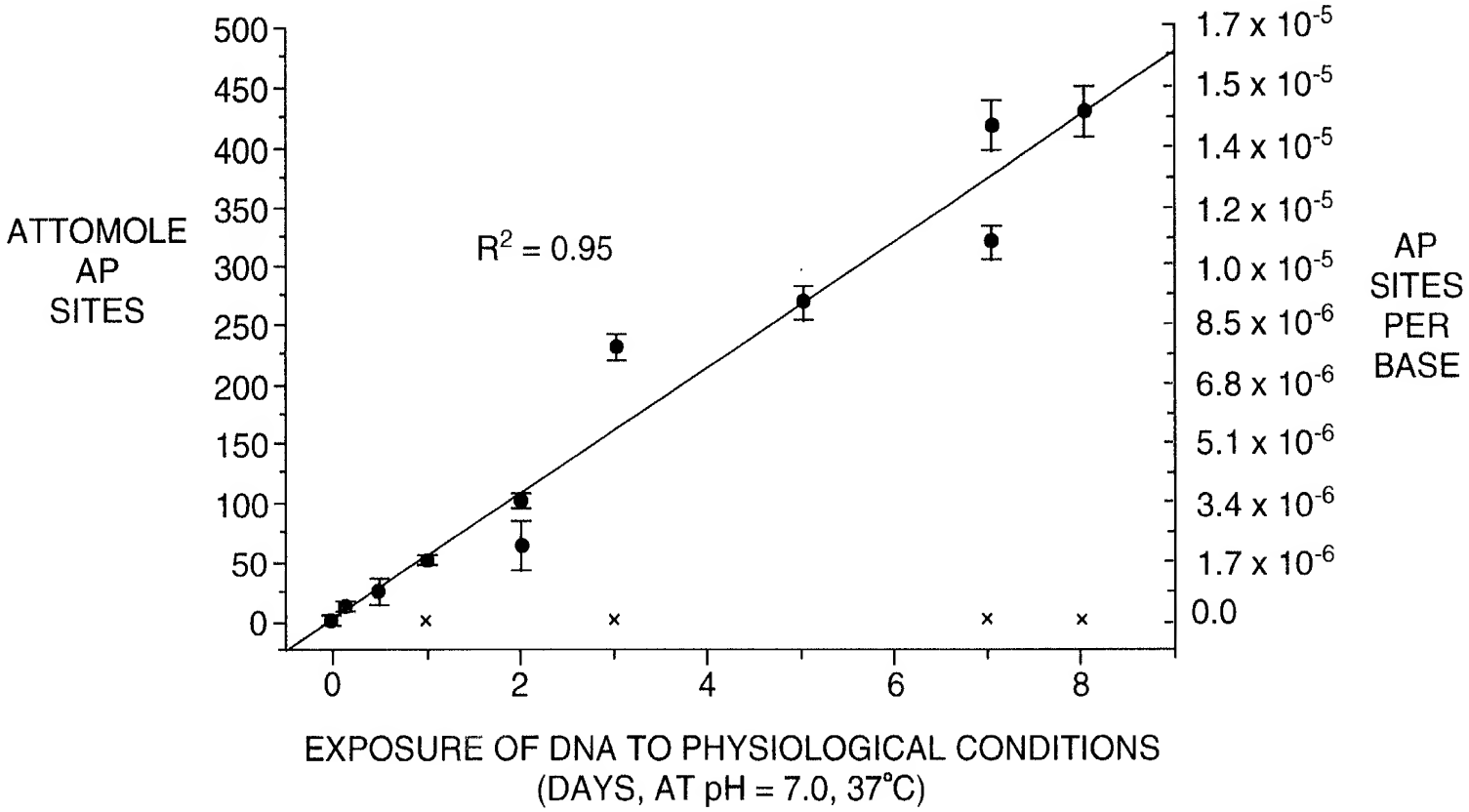

ATTOMOLE AP SITES
500
450
400
350
300
250
200
150
100
50
0
R^2 = 0.95
1.7 x 10^{-5}
1.5 x 10^{-5}
1.4 x 10^{-5}
1.2 x 10^{-5}
1.0 x 10^{-5}
8.5 x 10^{-6}
6.8 x 10^{-6}
5.1 x 10^{-6}
3.4 x 10^{-6}
1.7 x 10^{-6}
0.0
AP SITES PER BASE
0
2
4
6
8
EXPOSURE OF DNA TO PHYSIOLOGICAL CONDITIONS
(DAYS, AT pH = 7.0, 37°C)

FIG. 4B

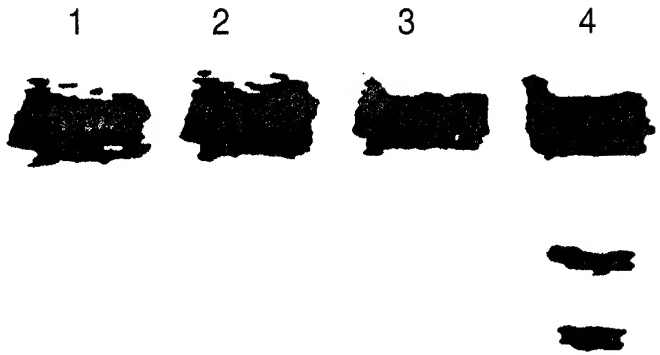


FIG. 5A

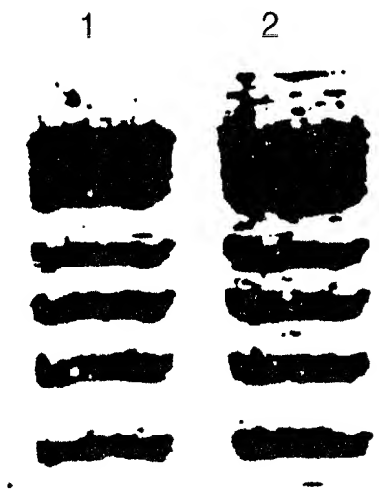


FIG. 5B

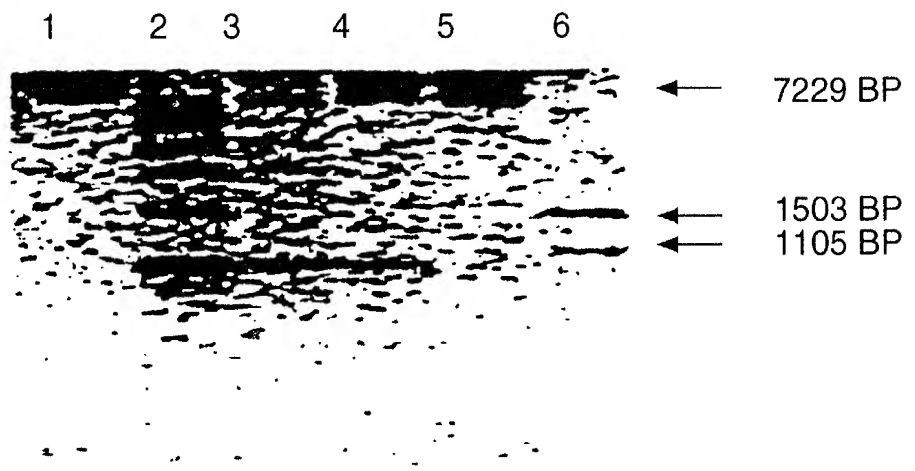


FIG. 5C

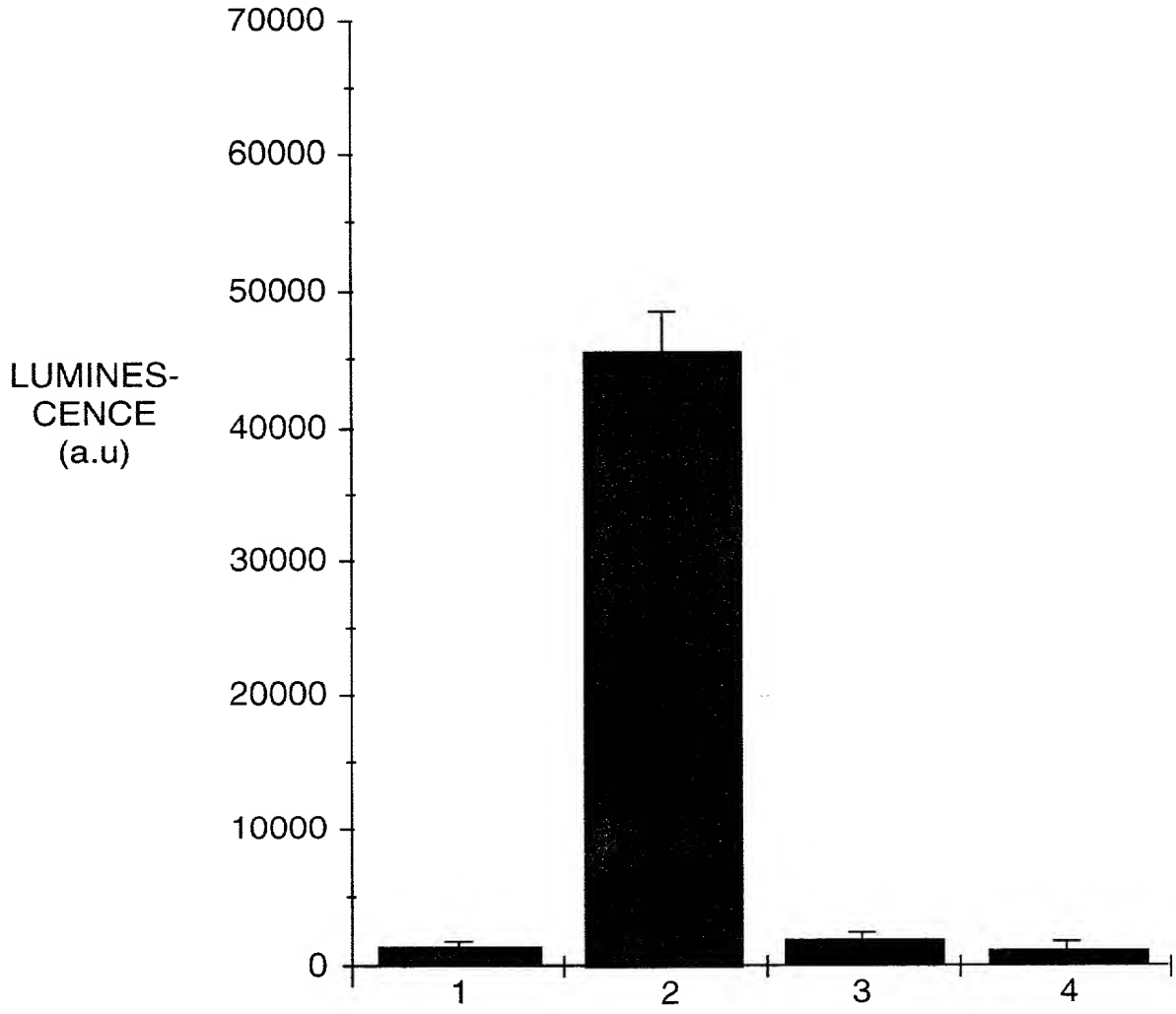

LUMINES-
CENCE
(a.u)
70000
60000
50000
40000
30000
20000
10000
0
1
2
3
4

FIG. 6

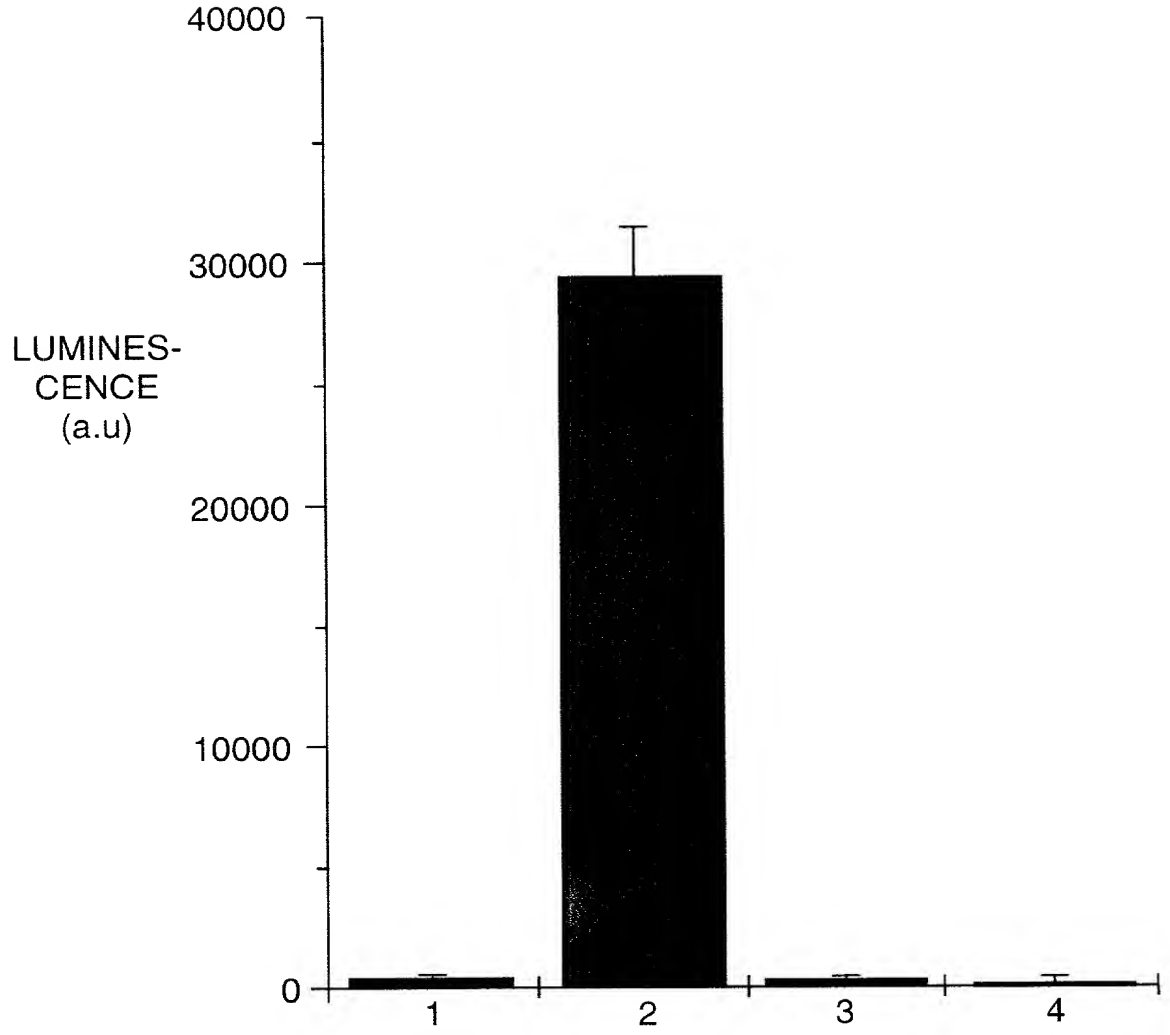
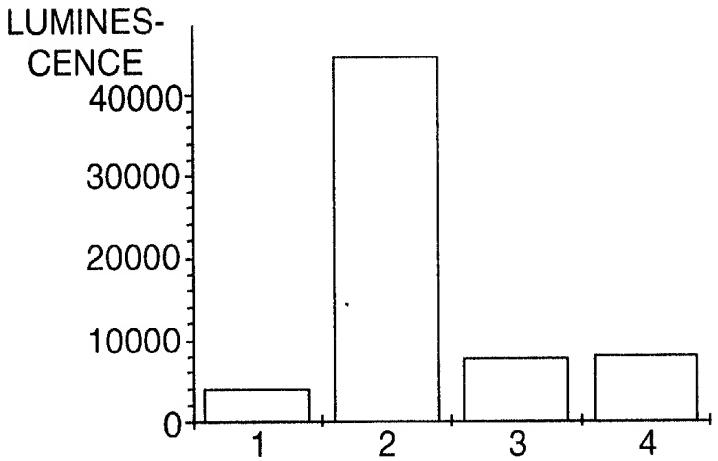


FIG. 7

DETECTION OF MISMATCHES FORMED BY HYBRIDIZING OLIGONUCLEOTIDES WITH M13 DNA AND EXPOSED TO MutY ENZYME



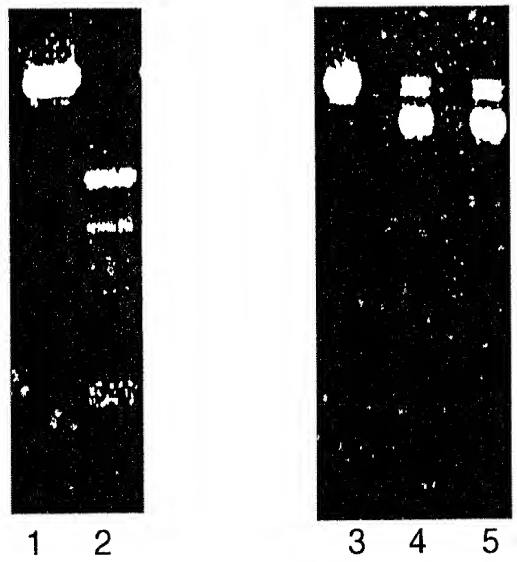
1= S.S. M13 DNA WITH ~ 1 A/G MISMATCH PER 2500 BASES, NO ENZYME

2= S.S. M13 DNA WITH ~ 1 A/G MISMATCH PER 2500 BASES, NO ENZYME

3= D.S. M13 DNA WITHOUT MISMATCH, NO ENZYME

4= D.S. M13 DNA WITHOUT MISMATCH, PLUS ENZYME

FIG. 8A



1= SINGLE STRANDED (S.S) M13 WITH 1 A/G MISMATCH PER 2500 BASES, NO ENZYME

2= S.S. M13 WITH 1 A/G MISMATCH PER 2500 BASES, PLUS ENZYME

3= S.S. M13 WITH 1 A/G MISMATCH PER 2500 BASES, NO ENZYME

4= DOUBLE STRANDED M13 WITHOUT MISMATCH, NO ENZYME

5= D.S. M13 WITHOUT MISMATCH, PLUS ENZYME

FIG. 8B

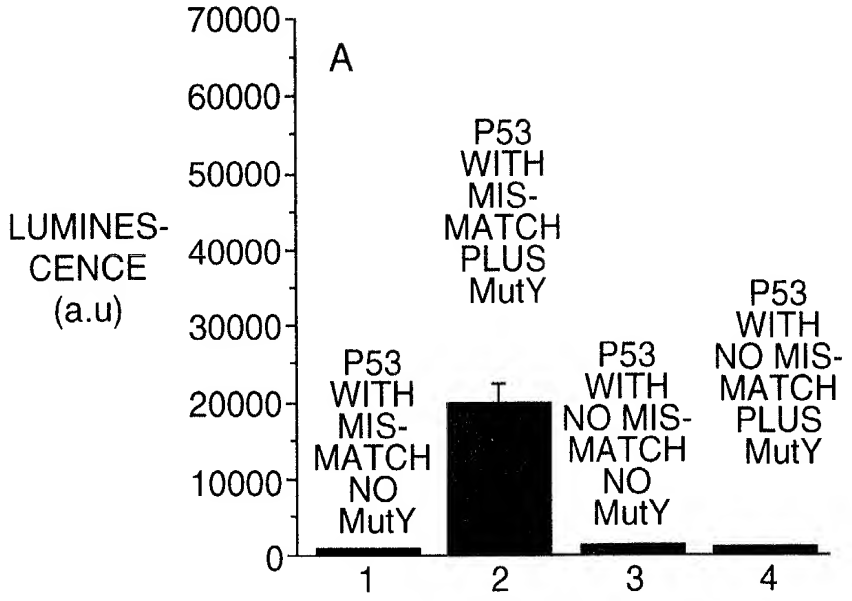

A
70000
60000
50000
40000
30000
20000
10000
0
LUMINES-
CENCE
(a.u)
P53
WITH
MIS-
MATCH
NO
MutY
P53
WITH
MIS-
MATCH
PLUS
MutY
P53
WITH
NO MIS-
MATCH
NO
MutY
P53
WITH
NO MIS-
MATCH
PLUS
MutY
1
2
3
4
P53 MUTATION DETECTION
ON NEUTRAVIDIN MICROPLATES

FIG. 9A

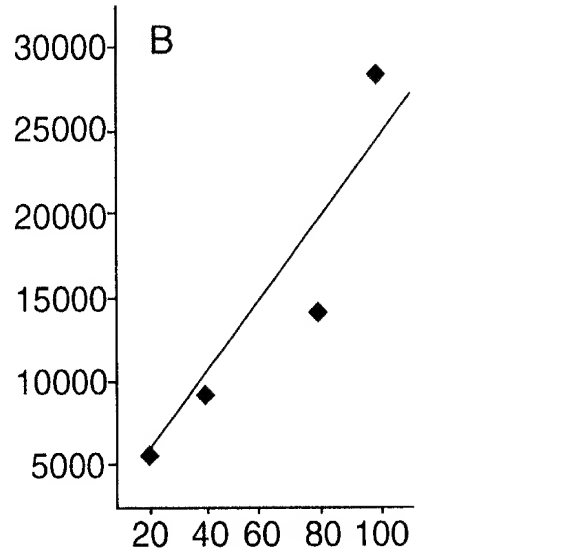

B
30000
25000
20000
15000
10000
5000
20
40
60
80
100
AMOUNT OF P53 SAMPLE APPLIED
ON NEUTRAVIDIN MICROPLATES (ng)

FIG. 9B

M13mp19 DNA TESTED.
A = DNA ALONE
B = DNA PLUS MUTY
C = DNA PLUS 5mM METHOXYAMINE PLUS MUTY
D = DNA PLUS 5mM AED PLUS MUTY
E = DNA PLUS 10mM AED PLUS MUTY
F = DNA PLUS 5mM BARP PLUS MUTY

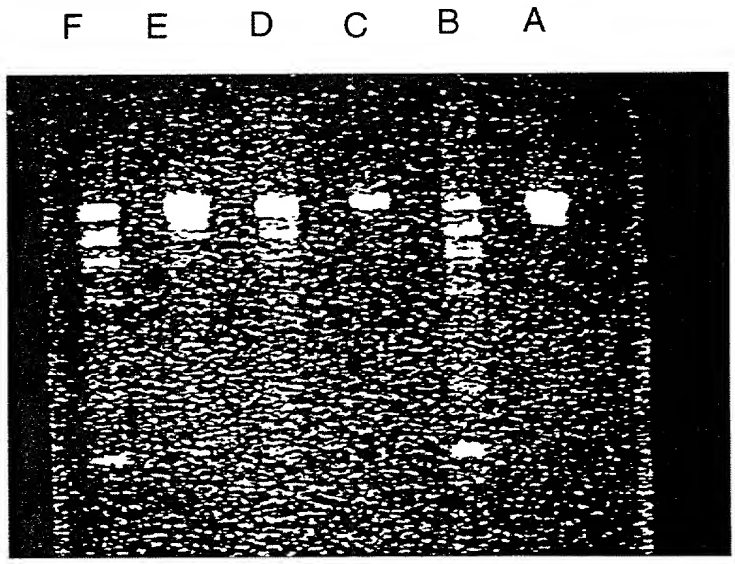


FIG. 10A

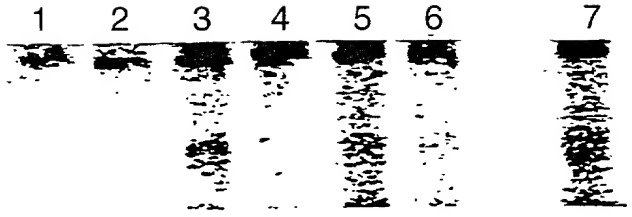
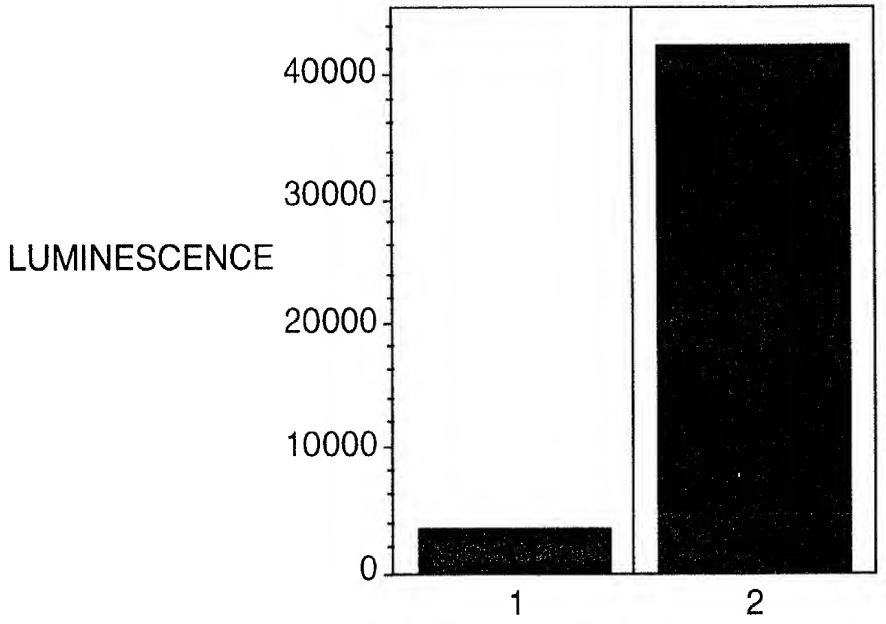


FIG. 10B



1: AED W/O ENZYME MutY
2: AED WITH MutY

FIG. 11

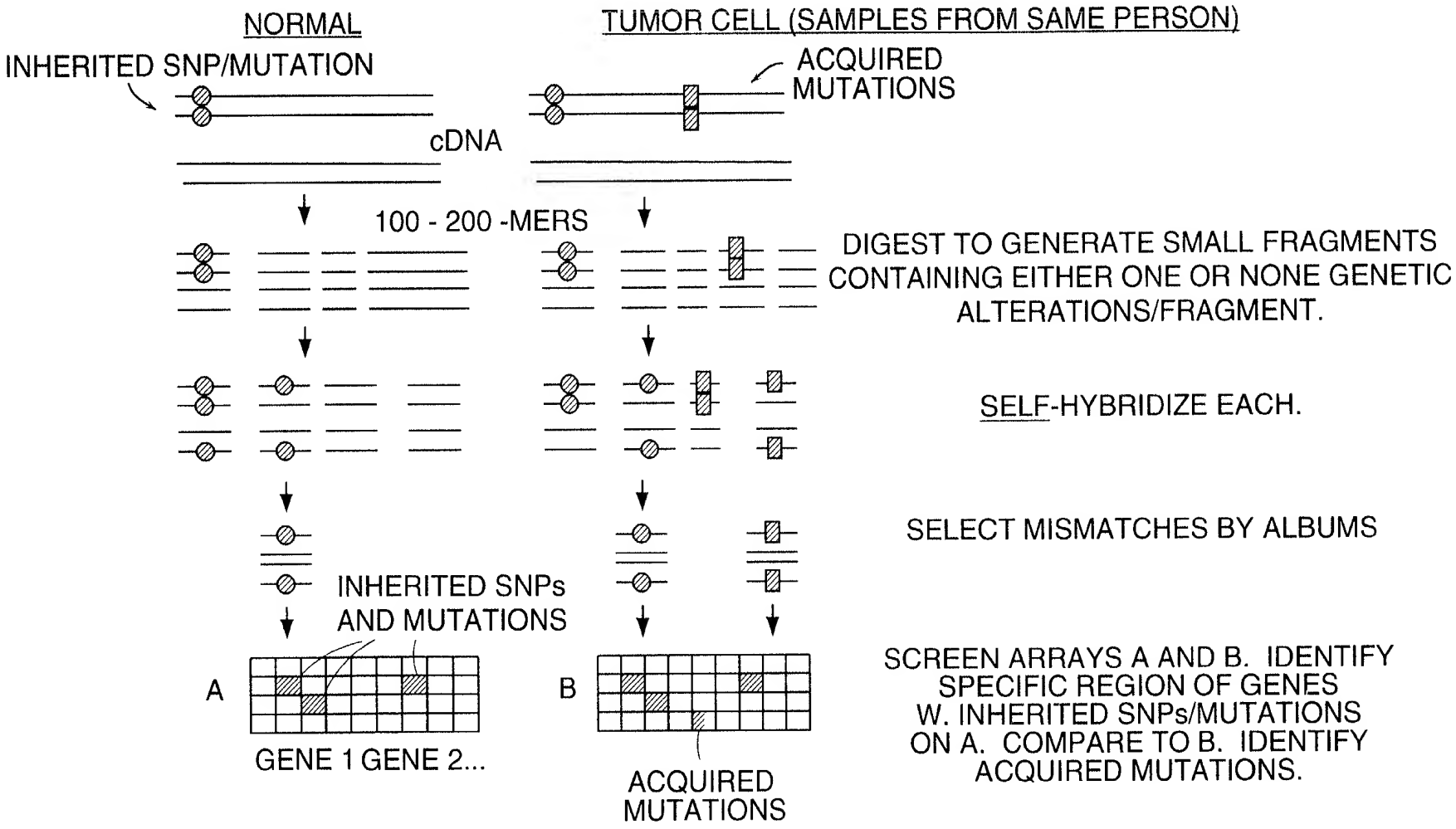

NORMAL
TUMOR CELL (SAMPLES FROM SAME PERSON)
INHERITED SNP/MUTATION
ACQUIRED MUTATIONS
cDNA
100 - 200 -MERS
DIGEST TO GENERATE SMALL FRAGMENTS CONTAINING EITHER ONE OR NONE GENETIC ALTERATIONS/FRAGMENT.
SELF-HYBRIDIZE EACH.
SELECT MISMATCHES BY ALBUMS
INHERITED SNPs AND MUTATIONS
A
B
GENE 1 GENE 2...
ACQUIRED MUTATIONS
SCREEN ARRAYS A AND B. IDENTIFY SPECIFIC REGION OF GENES W. INHERITED SNPs/MUTATIONS ON A. COMPARE TO B. IDENTIFY ACQUIRED MUTATIONS.

FIGURE 12

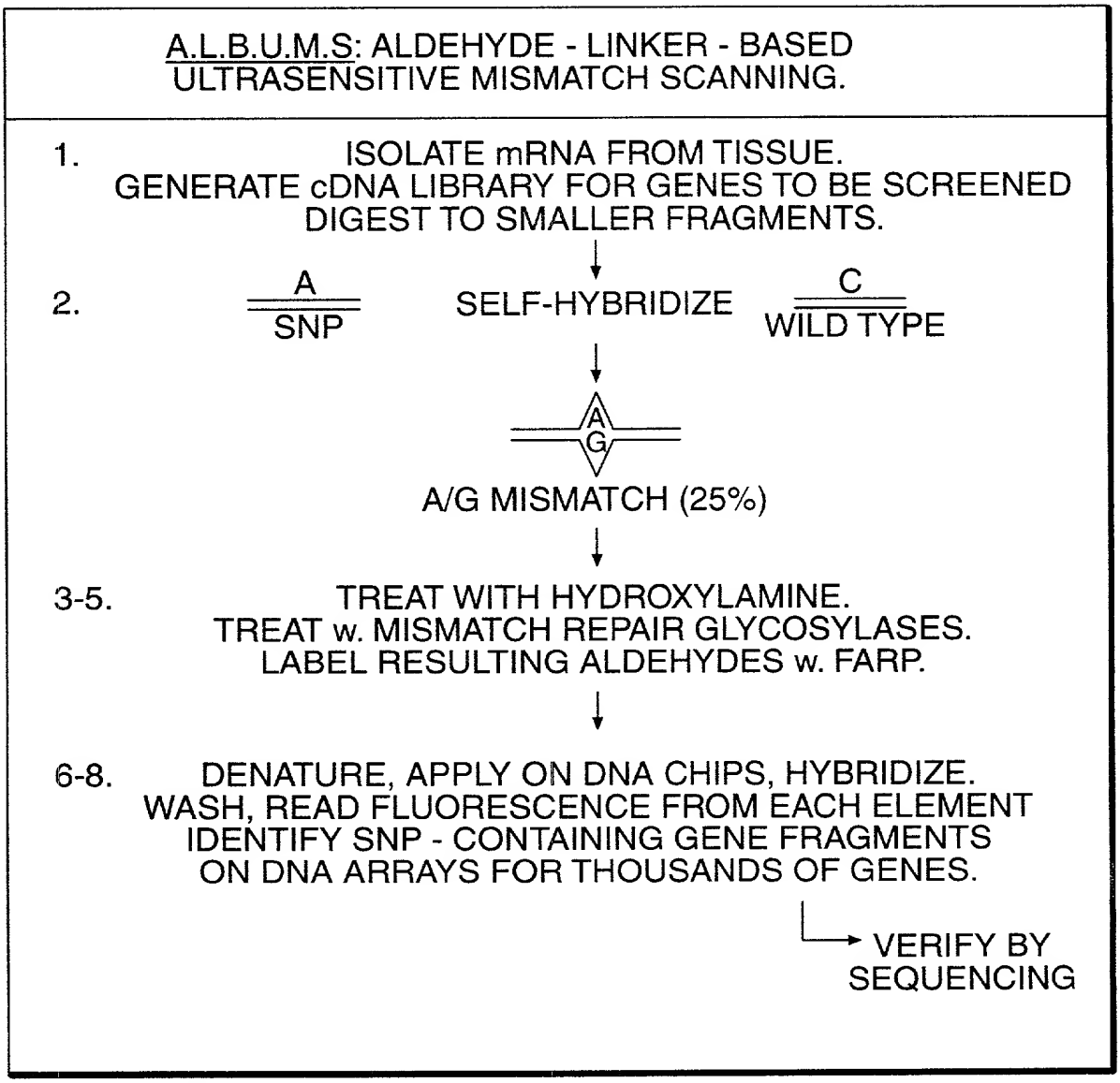


FIG. 13

SIMPLIFIED PROTOCOL TO DETECT SNPs
AND MUTATIONS ON DNA CHIPS.

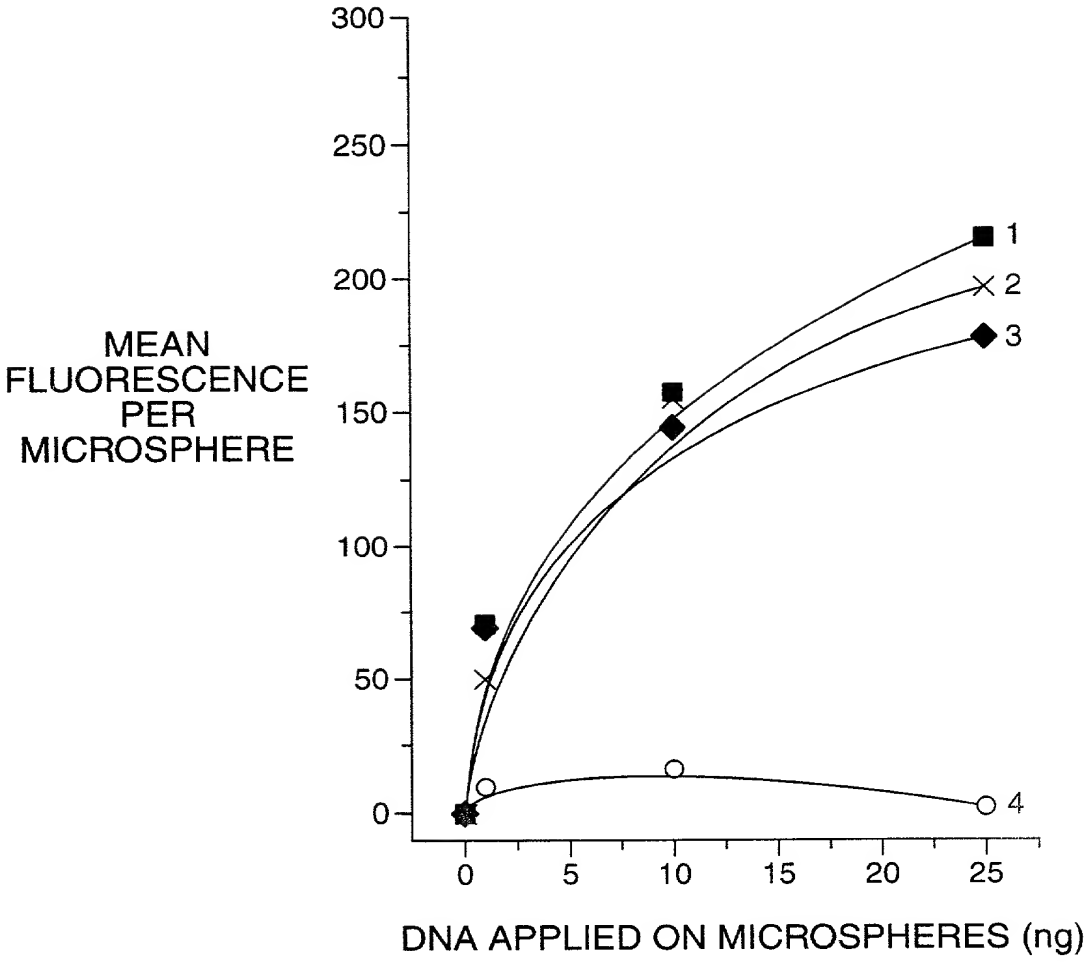

MEAN
FLUORESCENCE
PER
MICROSPHERE
300
250
200
150
100
50
0
0
5
10
15
20
25
1
2
3
4
DNA APPLIED ON MICROSPHERES (ng)

FIG. 14

MICROSPHERE-BASED
MUTATION SCANNING ARRAYS

EACH CODING SEQUENCE IS REPRESENTED BY OLIGONUCLEOTIDES ( ) SAMPLING THE mRNA AT REGULAR INTERVALS.

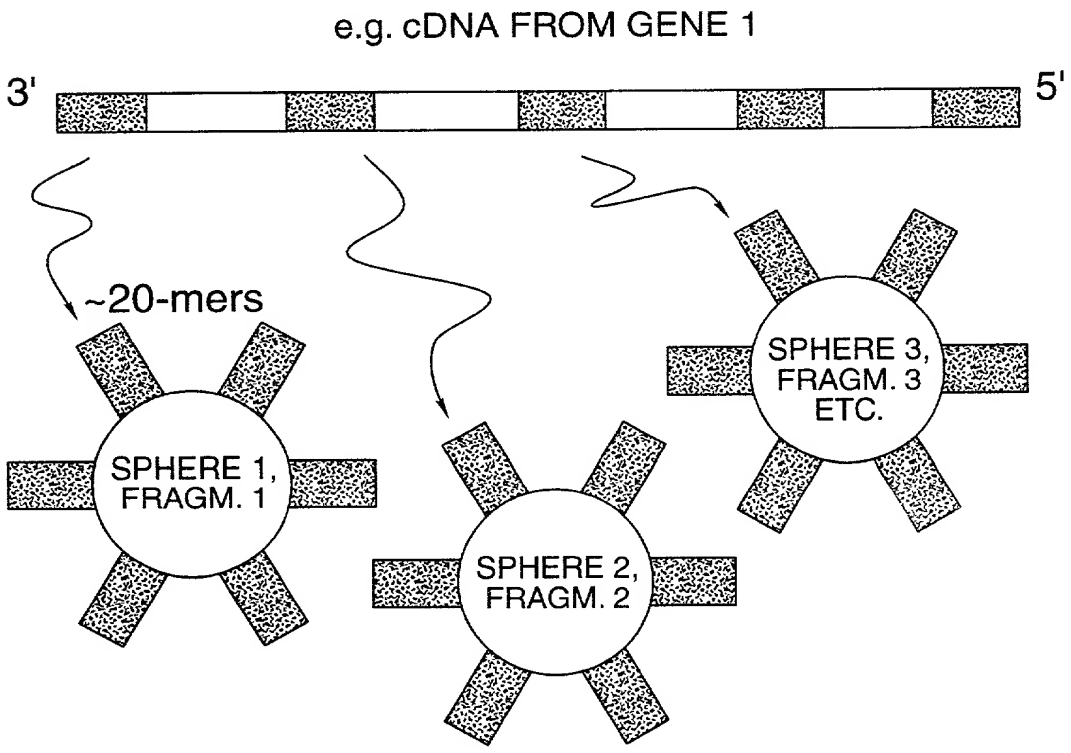


FIG. 15

THE OUTPUT INFO IS IN BINARY FORMAT